

human than the first adenovirus serotype resulting in a chimeric adenovirus that is less antigenic in a human than the first adenovirus serotype.

Sub D' 2. (Twice Amended) A recombinant vector derived from an adenovirus comprising at least one ITR and a packaging signal having [an] a first insertion site for a nucleic acid sequence of interest, and further having [an] a second insertion site for functionally inserting a gene encoding a penton and/or a hexon protein of a first serotype of adenovirus and having [an] a third insertion site for a gene sequence encoding a functional part of a fiber protein of a second adenovirus of a [different] second serotype, [wherein the] a gene encoding [the penton and/or hexon protein encodes] a penton and/or hexon protein from [an] the first adenovirus serotype inserted into the second insertion site, the first adenovirus serotype less antigenic in a human than the second adenovirus serotype, a gene sequence encoding at least a functional part of a fiber protein of the second adenovirus serotype inserted into the third insertion site, the gene sequence encoding at least a functional part of a fiber protein adapted to exhibit a desired tropism to a plurality of target cells in a host.

9. (Twice Amended) A method for producing a chimeric adenovirus having immunological properties determined by a hexon and/or penton of a first adenovirus serotype and a desired host range determined by a fiber of a second adenovirus serotype, said method comprising

providing a recombinant vector derived from an adenovirus comprising at least one ITR and a packaging signal having an insertion site for a nucleic acid sequence of interest, and further having an insertion site for functionally inserting a gene encoding a penton and/or a hexon protein of the first serotype of adenovirus and having an insertion site for a gene encoding a fiber protein of the second adenovirus;

inserting into said vector at least a functional part of a penton or hexon protein derived from the first adenovirus serotype having relatively low antigenicity as compared with the second adenovirus serotype,

selecting a fiber protein for a desired tropism to targeted tissue of a host, said fiber protein derived from the second adenovirus serotype;

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inserting into said vector at least a functional part of [a] the fiber protein [derived from the second adenovirus serotype having the desired host range];
transfected said vector in a packaging cell; and
producing chimeric viral particles.

Please add the following new claims:

13. A method for selecting and producing a chimeric adenovirus having a desired host range determined by at least one part of a fiber of a first adenovirus serotype and immunological properties determined by at least one part of at least one of a hexon or penton of a second adenovirus serotype, said method comprising

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providing a recombinant vector derived from an adenovirus comprising at least one ITR and a packaging signal, said recombinant vector having an insertion site for a gene of interest, said recombinant vector further having an insertion site for a nucleic acid encoding at least one part of a fiber protein of the first adenovirus serotype and having an insertion site for functionally inserting a nucleic acid encoding at least one part of at least one of a penton or a hexon protein of the second adenovirus serotype;

providing a nucleic acid library comprising a plurality of nucleic acids encoding a plurality of adenoviral proteins of a plurality of adenovirus serotypes, said plurality of nucleic acids flanked by restriction sites wherein said restriction sites correspond to said insertion sites in said recombinant vector;

inserting into said recombinant vector at least one first nucleic acid from said nucleic acid library, said at least one first nucleic acid obtained from the second adenovirus serotype and encoding at least one part of at least one of a penton or hexon protein, said penton or hexon protein having lower antigenicity relative to penton or hexon proteins of the first adenovirus serotype and conferring a viral particle having lower antigenicity;

inserting into said recombinant vector at least one second nucleic acid from said nucleic acid library, said at least one second nucleic acid obtained from the first adenovirus serotype and encoding at least one functional part of a fiber protein having the desired host

range;

providing at least one packaging cell;
transfected said recombinant vector into said at least one packaging cell; and
producing chimeric viral particles.

14. The method according to claim 13, further comprising inserting said gene of interest into said recombinant vector prior to said transfecting.

15. The method according to claim 14, wherein said providing a recombinant vector comprises providing an expression cassette for said gene of interest.

16. The method according to claim 1, wherein said providing a nucleic acid library comprises providing a plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes, and wherein said plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes are flanked by uniform restriction sites.
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17. The method according to claim 13, wherein said providing a recombinant vector comprises providing a vector lacking the E1 adenoviral genome.

18. The method according to claim 17, wherein said providing at least one packaging cell comprises providing at least one packaging cell selected from the group consisting of PER.C6, 911, 293, and E1 A549 cells.

19. The method according to claim 13, wherein said providing a recombinant vector comprises providing a recombinant vector derived from an adenovirus Sub-Group C serotype.

20. The method according to claim 19, wherein said adenovirus Sub-Group C serotype comprises one of Ad2 or Ad5.

21. The method according to claim 13, wherein said at least one first nucleic acid is obtained from an adenovirus Sub-Group B or C serotype.

22. The method according to claim 13, wherein said at least one second nucleic acid is obtained from an adenovirus Sub-Group B or C serotype.

23. The method according to claim 13, wherein said providing a recombinant vector comprises providing a vector selected from the group consisting of viral, plasmid, and cosmid vectors.

24. The method according to claim 13, wherein said at least one second nucleic acid obtained from the first adenovirus serotype comprises a nucleic acid encoding a knob protein of a fiber protein, and wherein said at least one first nucleic acid obtained from a second adenovirus serotype further comprises a nucleic acid encoding a base protein of a fiber protein and a shaft protein of a fiber protein.

25. The method according to claim 13, wherein said providing a nucleic acid library comprises providing nucleic acids carrying sequence mutations, and wherein said nucleic acids carrying sequence mutations encode proteins screened for characteristics selected from the group consisting of temperature stability, assembly, anchoring, redirected infection, and altered immune response.

26. The method according to claim 13, wherein said providing a nucleic acid library comprises providing nucleic acids encoding a plurality of adenoviral proteins obtained from a plurality of adenovirus serotypes selected from the group consisting of adenovirus Sub-Groups A, B, C, D, E, F, and G.

27. A library of chimeric adenovirus produced by the method according to claim 13.

28. A method of generating a library of chimeric adenoviruses, said method comprising:

providing a plurality of recombinant vectors derived from an adenoviral genome, each of said plurality of recombinant vectors having an insertion site for a nucleic acid encoding at least one part of a fiber protein of an adenovirus serotype having a desired host range and having an insertion site for functionally inserting a nucleic acid encoding at least one part of at least one of a penton or a hexon protein of a differing adenovirus serotype having predetermined antigenic properties;

providing a nucleic acid library comprising a plurality of nucleic acids encoding a plurality of adenoviral proteins of a plurality of adenovirus serotypes, said plurality of nucleic acids flanked by restriction sites wherein said restriction sites correspond to said insertion sites in said recombinant vector;

inserting into each of said plurality of recombinant vectors at least one first nucleic acid from said nucleic acid library encoding at least one functional part of a fiber protein obtained from an adenovirus serotype having a desired host range;

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inserting into each of said plurality of recombinant vectors at least one second nucleic acid from said nucleic acid library encoding at least one functional part of a penton or hexon protein of a differing adenovirus serotype having predetermined antigenic properties, said penton or hexon protein of each respective recombinant vector having lower antigenicity relative to penton or hexon proteins of the adenovirus serotype conferring the desired host range and resulting in a viral particle having lower antigenicity;

providing a plurality of packaging cells;
transfected said plurality of recombinant vectors into said plurality of packaging cells; and
producing a library of chimeric viral particles defined by differing fiber protein and penton or hexon protein adenovirus serotypes.

29. The method according to claim 28, wherein said producing a library of chimeric viral particles comprises generating a library of chimeric capsids.

30. The method according to claim 28, further comprising screening the produced chimeric viral particles for properties selected from the group consisting of target cell specificity, immunogenicity,

re-directed neutralization, re-directed hemagglutination, infection efficiency, toxicity, and pharmacokinetics.

31. The method according to claim 28, wherein said providing a nucleic acid library comprises providing a plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes, and wherein the plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes are flanked by uniform restriction sites.

32. A method for selecting and producing a chimeric adenovirus having a desired host range determined by at least one part of a fiber of a first adenovirus serotype, immunological properties determined by at least one part of at least one of a hexon or penton of a second adenovirus serotype, said method comprising

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providing a recombinant vector derived from the genome of adenovirus serotype 5, said recombinant vector comprising at least one ITR and a packaging signal and having an insertion site for a gene of interest, said recombinant vector further having an insertion site for a nucleic acid encoding at least one part of a fiber protein of the first adenovirus serotype and having an insertion site for functionally inserting a nucleic acid encoding at least one part of at least one of a penton or a hexon protein of the second serotype of adenovirus;

providing a nucleic acid library comprising a plurality of nucleic acids encoding a plurality of adenoviral proteins of a plurality of adenovirus serotypes, at least some of said plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes;

providing said plurality of nucleic acids flanked by restriction sites wherein said restriction sites correspond to said insertion sites in said recombinant vector and wherein the at least some of the plurality of nucleic acids encoding proteins of like functions for differing adenovirus serotypes are flanked by uniform restriction sites.; inserting into said recombinant vector at least one first nucleic acid from said nucleic acid library, said at least one first nucleic acid obtained from the second adenovirus serotype